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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/495,947 02/02/00 COLEMAN

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EXAMINER
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HM12/0723

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ART UNIT	PAPER NUMBER
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1633

DATE MAILED:

07/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

**Office Action Summary**

Application No.

09/495,947

Applicant(s)

COLEMAN ET AL.

Examiner

Christopher Drabik

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 June 2001.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-29 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☒ Interview Summary (PTO-413) Paper No(s). 12.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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### **DETAILED ACTION**

Applicants response to the Restriction Requirement has been received and entered as paper NO 11. The amendments included in applicants response have also been entered. The Restriction Requirement was discussed telephonically on June 7<sup>th</sup>, 2001, at which time Mary Goulet elected cancer as the first and second species of hapten to be examined.

#### ***In the Claims***

It is respectfully submitted that applicants consider rewriting claim 21 to read: "A method of eliciting [illiciting] an immune response..." to more clearly define the claimed subject matter.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim1-13 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites "...plurality of nucleocapsid monomers, the primary sequence of which..." Defining the composition in terms of a primary sequence is vague and indefinite because it is unclear what applicants consider as primary sequences. Claims 2-13 depend from, and are, therefore, bound to the limitations of, claim 1.

Claim1-13 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites "...derived from duck hepatitis B virus..." The term "derived" is vague and indefinite because it only defines a starting source of material and does not describe sufficiently the end product of any number of steps involved in generating the claimed composition.

Claims 14-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 14,17 and 21 are rejected for the reasons cited above over the use of "primary sequences." Claims 15 and 16 depend from claim 14. Claims 18-20 depend from claim17,

Claims 14-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 14, 17 and 21 are rejected for the reasons cited above over the use of the term "derived". Claims 15 and 16 depend from claim 14. Claims 18-20 depend from claim17. Claims 22 and 23 depend from claim 21.

Claims 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

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applicant regards as the invention. Claims 14, recites "... a composition comprised of a nucleic acid and ....protein monomers, the primary sequences of which..." It is unclear whether "the primary sequences" refers to the nucleic acid or the protein monomers, or both. Clarification is required. Claims 15 and 16 depend from claim 14.

Claims 17-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 17, 18 and 19 are unclear because the recitation "...said mixture" has no antecedent basis. Claim 20 depends from claim 17.

Claims 24-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 24 recites "...said hapten being associated with said duck HBcAg." The claim is vague and indefinite because the term "associated" does not clearly define the relation of the hapten and HBcAg.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 3, 5, 6, 8 -13, 14 -16, and 21 – 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the

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specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 2, 3, 5, 6, 8-13, 14-16 and 21-29 are broadly drawn to compositions comprising nucleocapsid monomers comprising one or two cancer haptens assembled to form a particle. Claim 5 further recites an unspecified nucleic acid. Claim 6 is drawn to said particle containing one cancer hapten and also comprising nucleic acid (s) 3-5 (SEQ IDs 6-19 are drawn to non-elected subject matter). Claim 7 specifies said particle comprising two cancer haptens

Regarding the breadth of the claims, it is important to note that the claim language does not place any significant limitation on the nucleocapsid monomer; the use of the phrase "derived from duck hepatitis B virus" provides little information regarding the biochemical structure of the claimed monomer of the

The nature of the claimed invention taken as a whole is drawn to methods of vaccination against cancer. While claims 2, 3, 5, 6, 8-13 and 21-29 are drawn to compositions, it is well established that the specification must teach those of skill in the art how to both make and use the invention as broadly claimed. In re Goodman, 29 USPQ2d at 2013 (Fed. Cir. 1994), citing In re Vaeck, 20 USPQ2d at 1445 (Fed. Cir. 1991). In further citing In re Vaeck the MPEP states: "When a compound or composition claim is limited by a particular use, enablement of that claim should be evaluated based on that limitation." Accordingly composition claims of the instant application have been examined in regards to enablement

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While the field of cancer vaccination is rapidly progressing, the ability to effectively vaccinate an individual either therapeutically or prophylactically against cancer remains unpredictable. In reviewing the general state of the art Bodey et al state:

"Animal models, albeit highly artificial, have yielded promising results. Clinical trials in humans , however, have been somewhat disappointing. Although general immune activation directed against target antigens contained within the cancer vaccine has been documented in most cases, reduction in tumor load has not been frequently observed, and tumor progression and metastasis usually ensue, possibly following a slightly extended period of remission. The failure of cancer vaccines to fulfill their promise is due to the very relationship between host and tumor: through a natural selection process the host leads to the selective enrichment of clones of highly neoplastically transformed cells, which apparently are so dedifferentiated that they no longer express cancer cell specific molecules".

The basis of treatment using vaccination involves the priming of the immune system to antigens which the body recognizes as other. A principal difficulty in generating an anti-cancer vaccine involves convincing the immune system that proteins present on cancer cells are indeed antigenic i.e. that self proteins should be targeted by immune response. While a number of antigenic determinants related to cancer have been discovered the ability to use these determinants to create a vaccine has not been forthcoming.

Bodey et al in further outlining the difficulties in developing an anti-cancer vaccine state: "There are many different approaches which have been devised to induce neoplastically transformed cell specific immune activation, but the main

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underlying difficulty remains the identification of specific antigenic determinants on the surface of cancer cells which could elicit a rejection strength cytotoxic T lymphocyte mediated immune response." Indeed, a considerable problem involved with developing a cancer vaccine is the identification of appropriate antigenic determinants which are broadly expressed in tumors, however, it is likely that antigenic determinants which elicit strong immune responses vary from patient to patient. Hence Dallal et al state: "Unique antigens, those expressed selectively in one patient's tumor and not in another's may be the most important targets for T-cell recognition... Shared tumor antigens are peptide epitopes that many patients with the same tumor type express. Known shared antigens are rarely found in all or even a majority of patients with a given tumor, and these antigens would not be expected to have equal importance for every patient."

Unpredictability present in the art places a burden upon the applicant to clearly demonstrate that an invention can function as claimed. The amount of experimentation required to enable an invention is generally held to be inversely proportional to the degree of unpredictability in the field. Given that the field of cancer vaccination has had little success in demonstrating therapeutic efficacy, claims directed to cancer vaccination bear the burden of providing sufficient evidence to show advances over the state of the art. In there disclosure applicants have not constructed a vaccine bearing a putative cancer antigen or demonstrated that an immune response in an animal could be achieved. Nor have applicants demonstrated in an art accepted cancer model that any sort of therapeutic response could be achieved. Further, no guidance regarding the



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construction of a cancer vaccine has been provided nor identification of any particular epitope which might function to provide therapeutic immunity. Given the state of the art, the degree of guidance, the scope of the claims and the lack of any working examples, the invention as claimed could not be practiced by one of skill in the art without significant and undue experimentation.

Claim 17-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for  $Mg^{2++}$  or SDS, does not reasonably provide enablement for other charged agents. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It is well known in the art that the core particles of hepatitis B viruses are difficult to disrupt. Protocols for human HBV core monomer generation routinely involve the use of a strong ionic detergent such as SDS. To the examiner knowledge, the use of high concentrations of magnesium to disrupt HBV core particles has not been previously demonstrated. Applicants have demonstrated in their examples the disruption of duck HBV core antigens using magnesium, however, it is unclear that other divalent cations would function in the same manner.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 10,-13, 24 , 25 and 27 rejected under 35 U.S.C. 102(b) as being clearly anticipated by Mason et al (Journal of Virology (1980) 36(3): 829-836)

Claim 1 of the instant application is broadly drawn to a composition comprising a plurality of duck HBV nucleocapsid protein monomers assembled to form a particle. As noted previously in this action the terms "primary sequences" and "derived from" as used in the claim provide little information in delineating the limitations of the claim. The claim reads on any nucleocapsid monomer from any source. The use of open language in the claim (comprising) broadly claims any composition having nucleocapsid protein monomers assembled to form particles. While the term "composition" implies that the hand of man was involved in the invention, and therefore the claim clears the requirements of 35 USC 101, the composition, nonetheless, reads on isolated wild type duck HBV. Claims 2 and 3 require that the composition include one or two haptens present on the nucleocapsid protein. Applicants define a hapten as: "a disease specific antigenic determinant identified by biochemical, genetic or computational means". (see page 11) In light of the species election, interpretation of these claims is limited to applicants election of cancer haptens. The nature of the claimed invention is such that the invention is drawn to the nucleocapsid protein duck HBV core antigen. It is likely that core **antigen** has multiple antibody binding sites, therefore, the wild type virus satisfies the limitation of containing haptens. Further, duck HBV is associated with hepatocellular carcinoma, anticipating the requirement of haptens associated with cancer.

Mason et al describe the isolation of a duck HBV The virus disclosed has essentially all of the properties and limitations of claims 1-6, 10,-13, 24 , 25 and 27.

**Conclusion**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher Drabik whose telephone number is 703-605-1156. The examiner can normally be reached on Monday-Friday from 9am to 5pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached on 703- 305-4051. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

Inquiries of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234. Questions regarding review of formality issues may be directed to Kim Davis, the patent analyst assisting in this application. She may be reached at 703-305-3015.

  
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